diseases other than cancer are not known. The work will be continued along these lines, and attempts will be made to find differences by means other than optical rotation.

Acknowledgments.—The able technical assistance of Miss Elouise Oliver is acknowledged. We appreciate also the coöperation of Drs. C. D. Howe and B. J. Trunnell of the Anderson Hospital in providing the blood samples.

HOUSTON, TEXAS

NOTES

8-Azaguanine Analogs[1,2]

BY CARL TABB BAHNER, DOROTHY ELLIS BILANCIO AND EMMA MARGARET BROWN

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The effects of 8-azaguanine[3] as an inhibitor of the growth of microörganisms and certain tumors led to a request that we prepare similar compounds for studies which might throw light on the relation of structure to biological activity. As one of the simplest possible changes we undertook to replace the oxygen atom by a sulfur atom. Klingsberg and Papa[4] have reported the use of a pyridine solution of P_2S_5 for replacing the oxygen atom in 3,5-diiodo-2-pyridone and other compounds which are soluble in pyridine. 8-Azaguanine is practically insoluble in pyridine, but dissolves in a hot solution of P_2S_5 in pyridine. 5-Amino-7-mercapto-1-v-triazolo(d)pyrimidine and 5,7-dimercapto-1-v-triazolo(d)pyrimidine have been prepared from 8-azaguanine by taking advantage of this fact.

5-Amino-7-mercapto-1-v-triazolo(d)pyrimidine.—Thirteen grams of 8-azaguanine was added rapidly to a solution of 27 g. of P_2S_5 in 300 g. of pyridine. As refluxing was continued the clear, brown solution began to deposit crystals. After 6 hours the hot mixture was poured into 640 ml. of boiling water. Upon cooling and filtering 10 g. of buff colored solid was obtained. The crude solid which consisted partly of a phosphorus-containing compound was treated with boiling water. The crystals which deposited on cooling the water were dissolved in hot 0.05 *N* KSH. The precipitate which appeared upon acidification of the KSH solution with acetic acid and cooling was dried with care to avoid atmospheric oxidation and the methanol soluble fraction was recrystallized to give 2 g. of a final product which decomposed at 270°. In paper chromatography using a solvent consisting of 60 ml. of water, 3.6 ml. of acetic acid and 300 ml. of *n*-butanol, the R_f was 0.57; ultraviolet absorption: at *p*H 10 log $E_{224\ m\mu}$ 4.132, log E_{325} 3.950; at *p*H 6.51 log E_{231} 4.097, log E_{341} 3.925. *Anal.* Calcd. for $C_4H_4N_6S$: C, 28.51; H, 2.39; N, 49.97. Found: C, 28.39; H, 2.45; N, 49.81.

5,7-Dimercapto-1-v-triazolo(d)pyrimidine.—The crude solid obtained by a single treatment of 13.0 g. of 8-azaguanine with P_2S_5 in pyridine was dissolved in hot 1:1 hydrochloric acid and thrown out of solution by neutralization with ammonia. Six and seven-tenths grams of the recrystallized material was added to a solution of 11.0 g. of P_2S_5 in pyridine. After refluxing the mixture for 6 hours it was poured into boiling water and the crystals which formed were recrystallized by dissolving in hot 1:1 HCl and neutralizing with ammonia; yield 1 g. The R_f for this compound, using butanol–acetic acid–water solvent, was 0.76; ultraviolet absorption: at *p*H 6.51 log E_{283} 4.153, log E_{343} 4.002; at *p*H 10.0 log E_{283} 4.076, log E_{343} 3.801. *Anal.* Calcd. for $C_4H_3N_5S_2$: C, 25.95; H, 1.63; S, 34.60. Found: C, 26.20; H, 1.88; S, 34.58.

Data on the biological effects of these compounds are to be reported elsewhere.

We are indebted to Dr. R. O. Roblin and Dr. J. M. Ruegsegger of Lederle Laboratories for the 8-azaguanine used in these experiments, to Oldbury Electro-Chemical Company for phosphorus pentasulfide, to Dr. Alfred Gellhorn of Columbia University Institute of Cancer Research for calling our attention to the need for substituted triazolopyrimidines in his study of the mechanism of action of 8-azaguanine, to Dr. Howard Skipper and Dr. Lee Bennett and their associates of Southern Research Institute for determining the ultraviolet absorption spectra of these compounds and screening them against certain tumors, and to Dr. Harry W. Galbraith of Galbraith Analytical Laboratories for the carbon, hydrogen, nitrogen and sulfur analyses.

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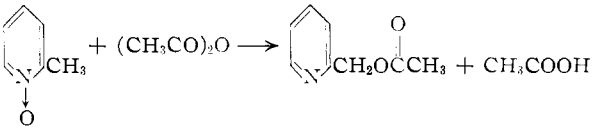
A New Synthesis of 1-(2-Pyridyl)-alkanols

BY O. H. BULLITT, JR., AND J. T. MAYNARD

RECEIVED DECEMBER 12, 1953

During an investigation of some of the reactions of pyridine N-oxides, a new rearrangement of alkyl-substituted pyridine oxides was encountered. The rearrangement is promoted by carboxylic acid anhydrides and results in the formation of an acylated 1-(2-pyridyl)-alkanol. For example, 2-methylpyridine oxide reacts with acetic anhydride to give 2-pyridylmethyl acetate



Proof of the proposed structure was provided by comparison of ultraviolet (Table I) and infrared spectra with those of known compounds, elementary analysis and preparation of the known picrate of the 2-pyridylmethanol obtained by saponification of the acetate.

(1) This research was supported in part by grants from the Damon Runyon Memorial Fund for Cancer Research and the National Institutes of Health, U. S. Public Health Service.

(2) Presented in part at the Southeastern Regional Meeting of the American Chemical Society, Auburn, Alabama, October 24, 1952.

(3) R. O. Roblin, Jr., J. O. Lampen, J. P. English, Q. P. Cole and J. R. Vaughn, Jr., THIS JOURNAL, **67**, 290 (1945).

(4) E. Klingsberg and D. Papa, *ibid.*, **73**, 4988 (1951).

TABLE I

ULTRAVIOLET ABSORPTION

	$\lambda_{max.}$, mμ	$\epsilon_{max.} \times 10^{-3}$	Solvent
Pyridine	246	1.84	CH_3OH
	251	2.45	
	257	2.71	
	263	1.84	
2-Methyl-5-Ethyl-pyridine	268	3.63	C_2H_5OH
	275	2.75	
Pyridine oxide	213	16.7	C_2H_5OH
	265	12.9	
4-Methylpyridine oxide	212	17.2	C_2H_5OH
	266	14.7	
5-Ethyl-2-pyridyl-methyl acetate	262		
	265	4.77	C_2H_5OH
	271		
5-Ethyl-2-pyridyl-methanol	263		
	267	3.64	C_2H_5OH
	273		
1-(2-Pyridyl)-ethanol	256		
	262	3.27	C_2H_5OH
	267		
2-Pyridol[a]	227	10	
	297	6.32	C_2H_5OH

[a] H. Specker and H. Gawrosch, *Ber.*, **75B**, 1338 (1942).

The reaction has been demonstrated for 2-methyl-, 4-methyl-, 5-ethyl-2-methyl- and 2-ethylpyridine oxides. In the latter case rearrangement takes place to yield 1-(2-pyridyl)-ethyl acetate rather than 2-(2-pyridyl)-ethyl acetate.

The reaction of quinaldine oxide with benzoyl chloride and sodium hydroxide, originally investigated by Henze[1] has recently been discussed by Pachter,[2] who concluded that the product was 2-quinolinemethyl benzoate. Pachter's interpretation of Henze's reaction is in accord with the results reported here.

Experimental

Pyridine N-Oxides.—The oxides were prepared by reaction of the appropriate pyridine with hydrogen peroxide in acetic acid using a procedure substantially identical with that described by Ochiai.[3] Pyridine oxide had b.p. 122–124° (5 mm.), m.p. 66° (lit.[4] 66–68°), and $n^{26}D$ 1.6118 (taken on the supercooled liquid); 2-methylpyridine oxide, b.p. 123° (9 mm.) and $n^{25}D$ 1.5854; 2-ethylpyridine oxide, b.p. 109–113° (4 mm.), $n^{25}D$ 1.5707; 2-methyl-5-ethylpyridine oxide, b.p. 147° (11 mm.), and $n^{26}D$ 1.5634.

4-Methylpyridine oxide had m.p. 186–188° after recrystallization from ethanol/ethyl acetate. Ultraviolet absorption confirmed its structure.

Anal. Calcd. for C_6H_7ON: C, 66.04; H, 6.46; N, 12.83. Found: C, 65.59; H, 6.55; N, 12.54.

5-Ethyl-2-pyridylmethyl Acetate.[5]—Acetic anhydride (125 ml.) was stirred at 60–65° while 34 g. of 5-ethyl-2-methylpyridine oxide was added dropwise in about 10 min. The temperature of the red solution was held at 60–65° for 1.5 hr., first by the use of an ice-bath and later by gentle heating. Acetic anhydride was removed by distillation and the residue fractionated to yield a main fraction (26.8 g.) which had b.p. 120–127° (5 mm.), $n^{25}D$ 1.5005.

Anal. Calcd. for $C_{10}H_{13}O_2N$: C, 67.01; H, 7.31; N, 7.82. Found: C, 67.56; H, 7.38; N, 8.33.

Infrared absorption of this compound indicated the presence of an aromatic nucleus (6.2–6.3 μ) and an ester group (C=O, 5.8 μ; C–O–C, 8.1 μ). Ultraviolet absorption confirmed the presence of an aromatic nucleus and ruled out the possibility of a pyridine oxide or a pyridone (see Table I).

5-Ethyl-2-pyridylmethanol.—An 8.0-g. sample of 5-ethyl-2-pyridylmethyl acetate was saponified by heating under reflux with 50 ml. of 10% sodium hydroxide. The alcohol was separated by extraction with methylene chloride. The dried methylene chloride solution was distilled to give 4.6 g. of colorless 5-ethyl-2-pyridylmethanol, b.p. 116–117.5° (5 mm.), $n^{25}D$ 1.5299.

Anal. Calcd. for $C_8H_{11}ON$: C, 70.04; H, 8.08; N, 10.22. Found: C, 70.00; H, 8.29; N, 11.06.

Infrared absorption of this compound indicated the presence of an aromatic nucleus (6.2–6.3 μ) and a primary hydroxyl group (3.1 and 9.3–9.5 μ). Ultraviolet absorption confirmed the presence of an aromatic nucleus and ruled out the possibility of a pyridine oxide or a pyridone (Table I).

2-Pyridylmethanol.—2-Methylpyridine oxide was rearranged in acetic anhydride essentially as described above. The crude 2-pyridylmethyl acetate, b.p. 112–117° (5 mm.), was saponified with sodium hydroxide to give 2-pyridylmethanol, b.p. 111–112° (15 mm.) (lit.[6] 112° (16 mm.)). The picrate was prepared in the usual way and recrystallized several times from ethanol, m.p. 159–161° (lit.[6] 159°).

1-(2-Pyridyl)-ethanol.—A sample of 2-ethylpyridine oxide was rearranged in a similar way to give 1-(2-pyridyl)-ethyl acetate, b.p. 89–93° (3 mm.), $n^{25}D$ 1.4913, yield 66%.

The ester was saponified to give a 60% yield of 1-(2-pyridyl)-ethanol, b.p. 85–89° (5 mm.), and $n^{25}D$ 1.5253. Infrared absorption of this compound indicated the presence of an aromatic nucleus (6.2–6.3 μ) and a secondary hydroxyl group (3.1 and 9.0–9.3 μ).

A chloroplatinate was prepared in the usual way, m.p. 169–172° dec.

Anal. Calcd. for $(C_7H_9NO)_2 \cdot H_2PtCl_6$: Pt, 29.8. Found: Pt, 29.88.

It will be noted that the physical constants observed for our 1-(2-pyridyl)-ethanol are quite different from those reported for the solid of indefinite melting point obtained by Pinner[7] and called 1-(2-pyridyl)-ethanol by him. It appears highly likely that Pinner actually had the corresponding pinacol, a possibility which he recognized.

The same alcohol was isolated from a similar reaction in which the acetic anhydride was replaced by propionic anhydride.

4-Pyridylmethyl Acetate—Treatment of 33.5 g. of methylpyridine oxide with acetic anhydride following the procedure outlined above yielded 24 g. of a liquid, b.p. 85–95° (4 mm.). This material was presumed to be 4-pyridylmethyl acetate, but a conclusive identification was not made.

(1) M. Henze, *Ber.*, **69**, 534 (1936).
(2) I. J. Pachter, THIS JOURNAL, **75**, 3026 (1953).
(3) E. Ochiai, *J. Org. Chem.*, **18**, 534 (1953).
(4) J. Meisenheimer, *Ber.*, **59**, 1848 (1926).
(5) O. H. Bullitt, Jr., U. S. Patent 2,663,711 (Dec. 22, 1953).
(6) C. D. Harries and G. H. Lenart, *Ann.*, **410**, 107 (1915).
(7) A. Pinner, *Ber.*, **34**, 4241 (1901); *Beilstein*, **21**, 50 (1910).

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1,2-Di-(2-pyridyl)-ethane[1,2]

BY PAUL G. CAMPBELL AND PEYTON C. TEAGUE

RECEIVED NOVEMBER 16, 1953

Edwards and Teague[3] obtained a compound $C_{12}H_{12}N_2$ as a by-product of the preparation of 2-pyridylmethanol by the air oxidation of 2-picolyllithium. This compound was not identified but was assumed to be 1,2-di-(2-pyridyl)-ethane. Thayer[4] later prepared the same compound by heating 2-picoline with sulfur.

In order to confirm the structure and to obtain the compound in good yield, a study was made of

(1) This work was supported in part by a Frederick Gardner Cottrell Grant from the Research Corporation.
(2) From the M.S. thesis of Paul G. Campbell, University of South Carolina.
(3) W. M. Edwards and P. C. Teague, THIS JOURNAL, **71**, 3548 (1949).
(4) H. I. Thayer, U. S. Patent 2,496,319, Feb. 7, 1950.